

11-28-03

1653

Docket No. 20784/6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Hans-Ulrich Demuth et al. ART UNIT: 1653  
SERIAL NO.: 10/082,001 CONFIRMATION NO.: 1724  
FILED: February 22, 2002 EXAMINER: Chih Min Kam  
FOR: **NEW EFFECTORS OF DIPEPTIDYL PEPTIDASE IV FOR TOPICAL USE**

<b>CERTIFICATE OF MAILING</b>	
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.	
By: <u>Sandra J. Wittrup</u> Sandra J. Wittrup	<u>November 26, 2003</u> Date

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Date: November 26, 2003

Pursuant to Applicant(s) duty of disclosure, the information listed in the attached form PTO-1449 is brought to the attention of the Examiner. Copies of the listed items are enclosed.

The citation of the listed items is not a representation that they constitute a complete or exhaustive listing of the relevant art or that the references are prior art. The items listed are submitted in good faith, but are not intended to substitute for the Examiner's search. It is hoped, however, that in addition to apprising the Examiner of these particular items, they will assist in identifying fields of search and in making as full and complete a search as possible.

The filing of this information disclosure statement is not an admission that the information cited herein is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

In accordance with the requirement under 37 C.F.R. 1.98 (3)(i), the following are concise explanations of the relevance, as presently understood, with regard to those items submitted herewith that are not in the English language:

I. LIST OF PATENTS, PUBLICATIONS OR OTHER INFORMATION

The patents, publications or other information submitted for consideration by the Office are listed on PTO-1449, attached hereto.

II. COPIES

- a. ☒ Submitted herewith is a legible copy of (i) each U.S and foreign patent; (ii) each publication or that portion which caused it to be listed; and (iii) all other information or that portion which caused it to be listed

III. CONCISE EXPLANATION OF THE RELEVANCE  
(check at least one box)

- a. ☐ Except as may be indicated below in (b), all of the patents, publications or other information are in the English language or were cited in an English language Search Report, a copy of which is attached hereto (concise explanation not required).
- b. ☒ A concise explanation of the relevance of all patents, publications or other information listed that is not in the English language is as follows:

**GERMAN LANGUAGE DE 198 26 972 A1** Applicants have relied on an English language abstract in determining that this patent apparently relates to the use of inhibitors (I) of dipeptidyl peptidase IV (DP IV) or analogous enzymes for inhibiting the activation and proliferation of keratinocytes (including malignantly transformed keratinocytes) and tumor cells derived from keratinocytes.

**GERMAN LANGUAGE WO 99/61431** Applicants have relied on an English language abstract in determining that this patent apparently relates to dipeptide compounds or compounds analogous to dipeptide compounds, which are made of an amino acid and a thiazolidine or pyrrolidine group, and to their salts. The invention further relates to the use of these compounds in the treatment of impaired glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, diabetic neuropathy and nephropathy as well as secondary diseases of diabetes mellitus in mammals.

- c. ☐ The following additional information is provided for the Examiner's consideration:

**FEES**

IV. THIS IDS IS BEING FILED UNDER 37 C.F.R. § 1.97(b)  
(check one box)

- a. ☐ within three months of the filing date of a national application (37 C.F.R. § 1.97(b) (1)). No fee or certification is required.
- b. ☐ within three months of the date of entry of the national stage as set forth in §1.491 in an international application (37 C.F.R. § 1.97(b) (2)). No fee or certification is required.
- c. ☒ before the mailing date of a first Action on the merits (37 C.F.R. § 1.97(b) (3)). No fee or certification is required. In the event that a first Office Action on the merits has been issued, please consider this IDS under 37 C.F.R. § 1.97(c) and see the certification under 37 C.F.R. § 1.97(e) below, or, if no certification has been made, charge our deposit account a fee in the amount of \$180.00 as required by 37 C.F.R. § 1.17(p).

V. THIS IDS IS BEING FILED UNDER 37 C.F.R. § 1.97(c):  
(check one box)

before the mailing date of a Final Office Action under 37 C.F.R. § 1.113 (See 37 C.F.R. § 1.97(c) (1)) or before the mailing date of a Notice of Allowance under 37 C.F.R. § 1.311 (See 37 C.F.R. § 1.97(c) (2)).

- a. ☐ No certification; therefore, a fee in the amount of \$180.00 is required by 37 C.F.R. § 1.17(p).
- or
- b. ☐ See the certification below. No fee is required.

VI. CERTIFICATION UNDER 37 C.F.R. § 1.97(e) (check only one box)

The undersigned hereby certifies that

- a. ☐ each item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS; or

- b. ☐ no item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application or, to the best of my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this statement.
- c. ☐ Some of the items of information were cited in a communication from a foreign Patent Office as indicated in the Form 1449 by those references having an asterisk(\*). As to this information, the undersigned certifies that each item of information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application not more than three months prior to the filing of this IDS. As to the remaining information, the undersigned hereby certifies that no item of this remaining information contained in the IDS was cited in a communication from a foreign Patent Office in a counterpart foreign application or, to the best of my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this statement.

- ☐ A check in the amount of \$180.00 is enclosed for the above-indicated fee. A duplicate copy of this paper is attached.
- ☒ No fee is required.

VII. THIS IDS IS BEING FILED UNDER 37 C.F.R. § 1.704(d) (PATENT TERM ADJUSTMENT)

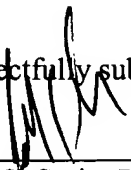
Applies to original applications (other than design) filed on or after May 29, 2000.

- a. \_\_\_\_\_ Each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart application and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the Information Disclosure Statement.
- b.   X   Enclosed herewith is form PTO-1449.
- c.   X   Copies of cited references are enclosed.
- d. \_\_\_\_\_ The listed references were cited in the enclosed International Search Report in a counterpart foreign application.

If the Examiner has any questions concerning this IDS, the Examiner is requested to contact the undersigned. If it is determined that this IDS has been filed under the wrong rule, the PTO is requested to consider this IDS under the proper rule (with a petition, if necessary) and charge any additional fees to Deposit Account No. 50-0369.

Respectfully submitted,

Date: November 26 , 2003



---

John C. Serio, Reg. No. 39,023  
BROWN RUDNICK BERLACK ISRAELS LLP  
Attorney for Applicants  
Customer No. 21710  
One Financial Center, Box IP  
Boston, MA 02111  
Tel: (617) 856-8238  
Fax: (617) 856-8201

**FORM PTO-1449**  
**INFORMATION DISCLOSURE STATEMENT**

**ATTY. DOCKET NO.**  
20784/6

**SERIAL NO.**  
10/082,001

**APPLICANT(S):** Hans-Ulrich Demuth et al.

**FILING DATE:**  
February 22, 2002

**ART UNIT:**  
1653

**UNITED STATES PATENT DOCUMENTS**

EXAM. INITIAL		DOCUMENT NUMBER	DATE	INVENTOR	CLASS	SUB CLASS	FIL. DATE IF APPR
	AA	5,705,483	01/06/1998	Galloway et al.	514	12	
	AB	5,827,898	10/27/1998	Khandwala et al.	514	734	
	AC	6,201,132 B1	03/13/2001	Jenkins et al.	548	535	04/21/99
	AD	6,303,661 B1	10/16/2001	Demuth et al.	514	866	04/24/97
	AE	6,500,804 B2	12/31/2002	Demuth et al.	514	19	12/31/02
	AF	6,319,893 B1	11/20/2001	Demuth et al.	514	2	11/20/01
	AG	6,011,155	01/04/2000	Villhauer	544	333	
	AH	6,107,317	08/22/2000	Villhauer	514	365	
	AI	6,110,949	08/29/2000	Villhauer	514	365	
	AJ	6,124,305	09/26/2000	Villhauer	514	272	
	AK	6,172,081	01/09/2001	Damon	514	307	
	AL	6,548,481 B1	04/15/2003	Demuth et al.	514	19	11/28/00
	AM	2001/0025023 A1	09/27/2001	Carr	514	2	

**FOREIGN PATENT DOCUMENTS**

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRAN Y/N
	BA	WO 99/61431	12/02/1999	PCT	C07D	277/04	Abstract Only-
	BB	EP 1 130 022 A1	09/15/2001	EPO	C07D	498/09	Y
	BC	WO 01/32624 A1	05/10/2001	PCT	C07D	217/04	Y
	BD	WO 01/09169 A2	02/08/2001	PCT	C07K	5/062	Y
	BE	WO 01/94310 A1	12/13/2001	PCT	C07D	209/12	Y

**Examiner:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**FORM PTO-1449**  
**INFORMATION DISCLOSURE STATEMENT**

**ATTY. DOCKET NO.**  
20784/6

**SERIAL NO.**  
10/082,001

**APPLICANT(S):** Hans-Ulrich Demuth et al.

**FILING DATE:**  
February 22, 2002

**ART UNIT:**  
1653

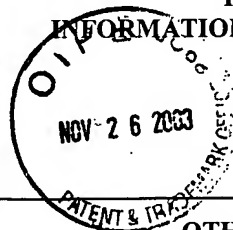
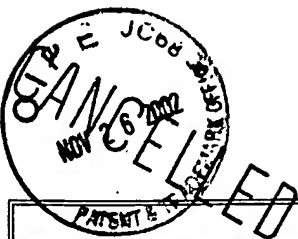
**FOREIGN PATENT DOCUMENTS**

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRAN Y/N
	BF	DE 198 26 972 A1	12/23/1999	Germany	A61K	38/05	N
	BG	WO 01/97808	12/27/2001	PCT	A61K	31/425	Y
	BH	WO 01/34594 A1	05/17/2001	PCT	C07D	401/06	Y
	BI	WO 00/10549	03/02/2000	PCT	A61K	31/00	Y
	BJ	WO 01/74299 A2	10/11/2001	PCT	A61K		Y
	BK	WO 02/20825 A1	03/14/2002	PCT	C12Q	1/00	Y
	BL	WO 01/89569 A1	11/29/2001	PCT	A61K	45/06	Y
	BM	WO 99/62914	12/09/1999	PCT	C07F	5/02	Y

**OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)**

CA	Bergmeier, Stephen C., <u>Tetrahedron</u> , Elsevier Science Ltd., "The Synthesis of Vicinal Amino Alcohols", Vol. 56, No. 17, (2000), pages 2561-2576.
CB	Kawamoto et al., <u>Tetrahedron Asymmetry</u> , Elsevier Science Ltd., "Enantioselective Synthesis of $\beta$ -Hydroxy Amines and Aziridines Using Asymmetric Transfer Hydrogenation of $\alpha$ -Amido Ketones", Vol. 11, No. 16 (2000), pages 3257-3261.
CC	Orskov, Cathrine et al., "Proglucagon Products in Plasma of Noninsulin-dependent Diabetics and Nondiabetic Controls in the Fasting State and after Oral Glucose and Intravenous Arginine" <u>J. Clin. Invest.</u> , Vol. 87, 1991, pages 415-423.
CD	Reinhold, D. et al., <u>Journal of Neuroimmunology</u> , "Inhibitors of Dipeptidyl Peptidase IV/CD26 Suppress Activation of Human MBP-Specific CD4 + T Cell Clones", (1998) 87: 203-209.
CE	Sengupta, et al., <u>Tetrahedron Letters</u> , Elsevier Science Ltd. "Amino Acid Derived Morpholine Amides for Nucleophilic $\alpha$ -Amino Acylation Reactions: A New Synthetic Route to Enantiopure $\alpha$ -Amino Ketones", Vol. 40, No. 21 (1999), pages 4107-4110.
CF	Stöckel-Maschek, A., et al., <u>Biochimica et Biophysica Acta</u> , "Thioxo Amino Acid Pyrrolidides and Thiazolidides: new Inhibitors of Proline Specific Peptidases", (2000) 1479: 15-31.
CG	Stryer, Lubert, <u>Biochemistry</u> , "Amino Acid Degradation and the Urea Cycle" (1975) pages 451-452.
CH	Mentlein et al., <u>Eur. J. Biochem</u> , Dipeptidyl-Peptidase IV Hydrolyses Gastric Inhibitory Polypeptide, Glucagon-Like Peptide-1(7-36)Amide, Peptide Histidine Methionine and is Responsible for Their Degradation in Human Serum. (1993), 214, pages 829-835.

**Examiner:** \_\_\_\_\_ **Date:** \_\_\_\_\_



<b>FORM PTO-1449</b> <b>INFORMATION DISCLOSURE STATEMENT</b>		ATTY. DOCKET NO. 20784/6	SERIAL NO. 10/082,001
		APPLICANT(S): <b>Hans-Ulrich Demuth et al.</b>	
		FILING DATE: February 22, 2002	ART UNIT: 1653
<b>OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)</b>			
CI	Wen-Tien Chen et al. "Seprase Complexes in Cellular Invasiveness", <i>Cancer and Metastasis Reviews</i> 22: 259-269, (2003).		
CJ	Victor A. Gault et al., "Glucose-Dependent Insulinotropic Polypeptide Analogues and Their Therapeutic Potential for the Treatment of Obesity-Diabetes", <i>Biochemical and Biophysical Research Communications</i> 308: 207-213, (2003).		
CK	Augustyns et al., <i>Eur. J. Med. Chem.</i> , "Pyrrolidides: Synthesis and Structure-Activity Relationship as Inhibitors of Dipeptidyl Peptidase IV", (1997), vol. 32, pages 301-309.		
CL	Lader, Malcolm H., MD, "Assessment Methods and the Different Diagnosis of Anxiety", <i>Journal of Clinical Psychopharmacology</i> , (1981), Vol. 1, No. 6, pp. 342-349.		
CM	Winslow, R., "Novartis Drug Alters Picture for Diabetes" <i>Wall Street Journal</i> , Wed., December 27, 2000, p. B2.		
CN	Ansorge, S., et al., "Membrane-bound peptidases of lymphocytes: Functional implications", <i>Biomed. Biochim. Acta</i> 50 (1991) 4-6, pp. 799-807.		
CO	Dodge, R.W., et al., "Folding and Unfolding Kinetics of the Proline-to-Alanine Mutants of Bovine Pancreatic Ribonuclease A," <i>Biochemistry</i> 1996, 35, pp. 1548-1559.		
CP	Demuth, Hans-Ulrich, "Recent Developments in Inhibiting Cysteine and Serine Proteases", <i>J. Enzyme Inhibition</i> , 1990, Vol. 3, pp. 249-278.		
CQ	Gomez, S., et al., "Relationship between endo- and exopeptidases in a processing enzyme system: Activation of an endoprotease by the aminopeptidase B-like activity in somatostatin-28 convertase", <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 85 pp. 5468-5472, August 1988.		
CR	Hegen, M., et al., "The T Cell Triggering Molecule Tp103 is Associated with Dipeptidyl Aminopeptidase IV Activity," <i>The Journal of Immunology</i> , vol. 144, pp. 2908-2914, No. 8, April 15, 1990.		
CS	Ishiura, S., et al., "Identification of a putative amyloid A4-generating enzyme as a prolyl endopeptidase," <i>Federation of European Biochemical Societies</i> , Vol. 260, No. 1, pp. 131-134, January 1990.		
CT	Kräusslich, Hans-Georg, et al., "Viral Proteinases", <i>Ann. Rev. Biochem.</i> 1988, 57 pp. 701-754.		
CU	Pederson, R.A., et al., "Improved Glucose Tolerance in Zucker Fatty Rats by Oral Administration of the Dipeptidyl Peptidase IV Inhibitor Isoleucine Thiazolidide", <i>Diabetes</i> , Vol. 47, August 1998 pp. 1253-1258.		
CV	Vanhoof, G., et al., "Proline motifs in peptides and their biological processing", <i>The FASEB Journal</i> , Vol. 9, June 1995, pp. 736-744.		
CW	Walter, R., et al., "Proline Specific Endo- and Exopeptidases", <i>Molecular &amp; Cellular Biochemistry</i> , Vol. 30, No. 2, April 18, 1980, pp. 111-127		
CX	Kessler, Von Horst, "Konformation und biologische Wirkung von cyclischen Peptiden", <i>Angew. Chem.</i> 94 (1982) pp. 509-520.		
<b>Examiner:</b>		<b>Date:</b>	

FORM PTO-1449

## INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.

20784/6

SERIAL NO.

10/082,001

APPLICANT(S): Hans-Ulrich Demuth et al.

FILING DATE:

February 22, 2002

ART UNIT:

1653

## OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)

CY

Kirschke, H. et al., "Proteinases 1: Lysosomal Cysteine Proteinases" *Protein Profile*, Vol. 2, Issue 14, 1995, pp. 1583-1634.

CZ

Yaron, A., et al., "Proline-Dependent Structural and Biological Properties of Peptides and Proteins" *Critical Reviews in Biochemistry and Molecular Biology*, 28(1), pp. 31-81 (1993).

CAA

Vallee et al., "Larval Development of Tribolium Confusum in the Presence of Non-Naturally Occurring Amino Acids", Database CAPLUS on STN, Accession No.: 1963:75103, *Annales de l'ACFAS* (1962), 28, p. 26-27 (abstract).

CAB

Holst, J. et al., "Inhibition of the Activity of Dipeptidyl-Peptidase IV as a Treatment for Type 2 Diabetes", *Diabetes*, 47, 11, Health & Medical Complete pp. 1663-1670, Nov. 1998.

Examiner:

Date: